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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,043	07/25/2003	Phillip Dan Cook	ISIS-5239	4045

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EXAMINER

RILEY, JEZIA

ART UNIT PAPER NUMBER

1637

DATE MAILED: 04/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/628,043	Applicant(s) COOK ET AL.	
	Examiner Jezia Riley	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32 and 34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32 and 34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/20/03</u> | 6) <input type="checkbox"/> Other: _____ |

[Handwritten signature]

DETAILED ACTION

1. Applicant's election of Group IV (claims 32 and 34) in the reply filed on 2/17/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821 (a)1 and (a)2. However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below:

In pages 23, 25, 31-34, nucleic acid sequences are cited without citing their corresponding SEQ ID NOs thus failing to comply with sequence rules as summarized above.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 32 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32 and 34 are indefinite because it is unclear whether the claims are drawn to methods of "detecting the presence or absence of an RNA in a biological sample," as recited in the preambles of claims 32 and 34, or to methods that merely require "contacting" a sample with a compound, as indicated by the single method step of the

claims. These do not make clear how or whether the contacting step actually results in "detecting the presence or absence" of RNA. Clarification is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 32 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses that the oligomeric compounds of the invention can be used in diagnostic, therapeutics as research reagents and kits (page 12). The specification discloses several examples of how to prepare some of these compounds. However there is no guidance as how one of ordinary skill in art will select a specific compounds from the one as broadly claimed in claims 32 and 34, for detecting the presence or absence of an RNA (any RNA) in a biological sample. One skilled in the art would recognize that the efficacy of an oligomeric analog or mimic for these uses depends critically on its having suitable conformation and flexibility, and also of its ability to penetrate cell membranes; and it is highly unpredictable whether a given oligonucleotide or mimic structure will permit binding to the target with high specificity and affinity. The efficacy of oligo analogs as hybridizing therapeutic agents depends unpredictably on the structures of the oligos. Uhlmann et al. (Chem. Reviews, 1990, 90,

pp.544-584) state that modified, nuclease-resistant oligos often have lower affinities for their target sequences than do natural DNA or RNA oligos (page 562, right col., 2nd paragraph; page 564, first full paragraph), that modified oligos may not penetrate cells as well as unmodified oligos (Page 568), and may fail to be taken up and transported into the target cells in amount capable of delivering a therapeutic benefits (page 567). In view of the breadth of the claims, which encompass an immense number of oligo mimic compounds of unknown activity; given that it is impossible to predict which of the multitude of oligo mimic structures encompassed by the claims would be able to bind successfully to a complementary nucleic acid or to protein with high affinity and specificity; and given the lack of guidance in the specification regarding how to select which of the specific oligos mimic structures encompassed by the claims could be made and used with a reasonable expectation of success, undue experimentation is required to make and use the invention as broadly claimed. Further synthesis where $R_A = (CH_2-CH_2-Q)_x$ has no guidance in the disclosure as filed and is therefore purely an invitation to experiment and therefore has unpredictable result without undue experimentation because these substituents will have a formula as follow:

$-CH_2-CH_2-O-O-C(X)-N(R_{1b})(R_{1c})$, or $CH_2-CH_2-O-N-C(X)-N(R_{1b})(R_{1c})$, for example, and a O-O or O-N bond is well known to be highly reactive and therefore require detailed chemical synthetic procedural guidance to prevent their undesired reaction during protection/deprotection reactions.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,803,198 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both claiming a method for detecting the presence or absence of an RNA in a biological sample comprising contacting said sample with compounds which have identical scope.

8. No claim is allowed.


9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786.

The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Monday, April 11, 2005



JEZIA RILEY
PRIMARY EXAMINER